The high sensitivity and negative predictive value (NPV) for systemic lupus erythematosus (SLE) makes the ANA test a good "rule out" test to essentially exclude this disorder if it is negative.[5] Indeed, the most recent European League Against Rheumatism/American College of Rheumatology guidelines for the diagnosis of SLE mandates a positive ANA (≥1:80) on the HEp-2 substrate to be considered for this diagnosis.[6] Sensitivities for detecting other AADs is low-moderate at best; yet also demonstrates very high NPVs.[7] Unless there has been a significant change in clinical picture or there is a suspicion of a laboratory issue, there is little value in repeating an ANA that is initially negative.[8]

A pitfall is that ANA is a screening test and may, in rare instances, miss low-level specific autoantibodies/anti-extractable nuclear antigens (ENAs) if more sensitive assays are not performed,[9] or miss anti-ENA that do not produce a characteristic ANA pattern e.g., anti-Ro52. Therefore, the substrate should be specified in the report since substrates such as the HEp-2000® (Immunoconcepts) which has transfected Ro60 increase the detection of anti-Ro60 and hence, a negative result makes the presence of anti-Ro60 less likely.[10]

If there is a high clinical suspicion for an AAD, the clinician should request further anti-ENA tests and the overall clinical picture and physician's interpretation of the patient should prevail. This is especially of importance since commercial HEp-2 substrates, whilst generally demonstrating excellent inter-assay and inter-laboratory agreement, display subtle staining differences that affect the microscopist's final interpretation.[11] The significance of low levels of anti-ENA with negative ANA is not well established.

To conclude, clinicians should be aware of the value, implications and pitfalls of a negative ANA result when considering AADs. They should also be aware of their laboratory's definitions of a "negative" ANA result, the substrate used and whether they report non-nuclear patterns which may have important implications for their patients. Importantly, the overall clinical picture of the patient should be taken into considerations when deciding on the relevancy of a negative ANA test.

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Conflict of interests

None declared.

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How do Spanish Rheumatologists handle referral? Survey of knowledge and approach before and after a training workshop☆

¿Cómo manejan la remisión los reumatólogos españoles? Encuesta de conocimientos y abordaje antes y después de un taller formativo

Dear Editor,

The aim of rheumatoid arthritis (RA) treatment is to achieve remission, but the criteria by which to establish remission are varied, complex, and unequally stringent[1], with the consequent complication of management. The main criteria are the cut-off points of composite indices (DAS28, SDAI, or CDAI), Boolean ACR/EULAR criteria, remission without treatment, or ultrasound remission[2]. Once remission is achieved, guidelines recommend dose reduction without discontinuing any drug (ACR[3]), tapering glucocorticoids initially and then biologic therapy (EULAR[1]), or tapering glucocorticoids (not classic DMARDs) and establishing a biologic therapy dose reduction plan (SER[4]).

Two years ago, we set out to analyse rheumatologists' knowledge regarding RA remission and its influence on therapeutic management in the outpatient setting. The rheumatologists completed a two-fold survey (Appendix B. Supplementary Material) before and 3 months after attending four scientific workshops on remission and management of patients in remission (including the RedoSER tool)[5]. Respondents were deemed to have elevated knowledge when ≥70% answered correctly; a 10-point increase or decrease in correct answers before and after the workshop implied variation.

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The results indicated that Spanish rheumatologists possess adequate knowledge of remission (prior to the workshop, at least 70% answered 67% of the questions correctly) and that a very high percentage of these specialists consider that the assessment of remission should include imaging, patient perspective, and biomarkers. Remission is largely evaluated by means of the DAS28 or its components and very little using imaging or PRO (patient-dependent variables). Especially noteworthy is the similarity of the responses and the scant change of opinion following the workshops. The only two remission questions that changed were the inclusion of seroconversion in the definition (change from 14% to 29%) and the use of the CDAI (change from 22% to 38%) (Appendix B. Supplementary material).

As regards management once remission is attained, the factors the rheumatologists valued most to decide whether or not to lower the dose of biologic therapy in patients in remission are: previous failure of biologics, poor prognostic factors, presence of Power Doppler signal, monotherapy, and being on glucocorticoids. Some Spanish rheumatologists use ultrasound in certain cases to reduce biologics, but do not generally use drug levels or the RedoSER tool. The only remission management questions that changed after the workshops had to do with the importance given to low-dose glucocorticoids, the presence of high activity at the time of biologic initiation, and disease duration <1–2 years.

The main changes in decision-making following the workshops were an increase in the use of ultrasound to determine a downward titration of biologic dose, and increased use of the RedoSER tool (unknown to 54%). According to rheumatologists' comments, this should include, among others, the risk of infection, drug or antibody levels, and calprotectin, a biomarker that correlates positively with inflammatory activity and increased radiographic progression[6] (Appendix B. Supplementary material).

Despite its limitations, this work provides interesting new insights into rheumatologists' doubts surrounding remission, its influence on therapeutic decision-making, and the need to individualise the therapeutic target during remission[7]. Finally, the workshops have contributed to increased the use of ultrasound and RedoSER for decision-making and brought about changes in motivation for lowering doses.

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Conflict of interest

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Appendix A. Grupo de trabajo Destino Remisión (Destination Referral Working Group)

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Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.reuma.2021.08.002.

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